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April 3, 2013

Via Federal Express

Document Processing Center (Mail Code 7407M)
Room 6428
Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1201 Constitution Ave., NW
Washington, DC 20004

Dear 8(e) Coordinator:

8EHQ-12-18717A
Generic Name: Substituted Nitrogen Containing Heterocycle

This letter is to inform you of the results of the developmental toxicity study with the above referenced R&D test substance. The test substance is an R&D substance and to the best of our knowledge not on the public inventory.

The objectives of this study were to determine the potential of the test substance to induce developmental toxicity. The test substance in the vehicle (0.5% methylcellulose [4000 cps] with 0.1% Tween® 80) was administered orally by gavage to 3 groups of 22 time-mated female New Zealand White [Hra:(NZW)SPF] rabbits once daily from gestation days 7 through 28. Dosage levels were 10, 30, and 120 mg/kg/day administered at a dosage volume of 10 mL/kg. A concurrent control group of 22 time-mated females received the vehicle on a comparable regimen. All animals were observed twice daily for mortality and moribundity. Clinical observations, body weights, and food consumption were recorded at appropriate intervals. On gestation day 29, a laparohysterectomy was performed on each surviving female. The uteri, placentae, and ovaries were examined, and the numbers of fetuses, early and late resorptions, total implantations, and corpora lutea were recorded. Gravid uterine weights were recorded, and net body weights and net body weight changes were calculated. Selected organs/tissues from all animals were collected, weighed, and preserved in 10% neutral-buffered formalin. From these organs/tissues, the stomach, kidney, urinary bladder, liver, and all gross lesions were examined microscopically from all animals. The fetuses were weighed, sexed, and examined for external, visceral, and skeletal malformations and developmental variations.

One female in the 120 mg/kg/day group was euthanized in extremis on gestation day 25 and 1 female in the 30 mg/kg/day group and 3 females in the 120 mg/kg/day group aborted on gestation day 25, 26, or 28 following body weight losses (up to 18.4%) with corresponding reductions in food consumption and increased incidence of decreased defecation and small feces. The abortions in the 120 mg/kg/day group were considered secondary to the body weight losses and reduced food consumption. Based on the absence of morbidity or similar effects on body weight and food consumption for surviving females at 30 mg/kg/day and the occurrence of an abortion for a single female in the control group (noted with similar effects on body weight and food consumption), the abortion in the 30 mg/kg/day group was not considered to be test substance-related. Slightly increased incidences of decreased defecation and small feces were noted for surviving females in the 10, 30, and 120 mg/kg/day groups compared to the control group generally throughout the treatment period, . Test substance-related centrilobular hepatocellular necrosis was noted in the liver at dosage levels ≥30 mg/kg/day, and tubular degeneration and dilatation were present in the kidney of the 120 mg/kg/day group.

COMPANY SANITIZED

Sincerely,